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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,629	12/16/2005	Peter Heegaard	63528(45579)	9252
21874 7590 10/20/2010 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
SCHLIENTZ, LEAH H				
ART UNIT		PAPER NUMBER		
1618				
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10/20/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/536,629

**Applicant(s)**

HEEGAARD ET AL.

**Examiner**

Leah Schlientz

**Art Unit**

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 July 2010.  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-58 is/are pending in the application.  
4a) Of the above claim(s) 19-46 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-18 and 47-58 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☒ The drawing(s) filed on 26 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:  
1. ☒ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO/SB-08)  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_  
Paper No(s)/Mail Date \_\_\_\_\_

## **DETAILED ACTION**

### ***Acknowledgement of Receipt***

Applicant's Response, filed 7/28/2010, in reply to the Office Action mailed 1/29/2010, is acknowledged and has been entered. Claims 1, 6-8 and 11-18 have been amended. Claims 47-58 are newly added. Claims 1-58 are pending, of which claims 19-46 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1-18 and 47-58 are readable upon the elected invention and are examined herein on the merits for patentability.

### ***Response to Arguments***

Any rejection not reiterated herein has been withdrawn as being overcome by amendment.

Applicant's arguments have been fully considered but they are not persuasive, for reasons set forth hereinbelow.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-18 and 47-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomalia *et al.* (US 5,714,166) in view of Aldrich Technical Publication, 1997.

Tomalia discloses dendritic polymer conjugates which are composed of at least one dendrimer in association with at least one unit of a carried material, where the carrier material can be a biological response modifier, have been prepared. The conjugate can also have a target director present, and when it is present then the carried material may be a bioactive agent (abstract). The dendrimers for use in the conjugates of the present invention, can have terminal groups which are sufficiently reactive to undergo addition or substitution reactions. Examples of such terminal groups include amino, hydroxy, mercapto, carboxy, alkenyl, nitrile, allyl, vinyl, amido, halo, **urea**, oxiranyl, aziridinyl, etc. The dendrimers differ from conventional star or star-branched polymers in that the dendrimers have a greater concentration of terminal groups per unit of molecular volume than do conventional extended star polymers having an equivalent number of core branches and an equivalent core branch length. Thus, the density of terminal groups per unit volume in the dendrimer usually is at least

1.5 times the density of terminal groups in the conventional extended star polymer, preferably at least 5 times, more preferably at least 10 times, most preferably from 15 to 50 times. The ratio of terminal groups per core branch in the dense polymer is preferably at least 2, more preferably at least 3, most preferably from 4 to 1024. Preferably, for a given polymer molecular weight, the molecular volume of the dense star polymer is less than 70 volume percent, more preferably from 16 to 60, most preferably from 7 to 50 volume percent of the molecular volume of the conventional extended star polymer (column 29-30).

A "dendritic polymer" is a polymer exhibiting regular dendritic branching, formed by the sequential or generational addition of branched layers to or from a core. The term "dendritic polymer" encompasses "dendrimers," which are characterized by a core, at least one interior branched layer, and a surface branched layer. A "dendron" is a species of dendrimer having branches emanating from a focal point which is or can be joined to a core, either directly or through a linking moiety to form a dendrimer. Many dendrimers comprise two or more dendrons joined to a common core. However, the term dendrimer is used broadly to encompass a single dendron. Dendritic polymer includes, but is not limited to, symmetrical and unsymmetrical branching dendrimers, cascade molecules, arborols, and the like, though the most preferred dendritic polymers are dense star polymers. The PAMAM dense star dendrimers disclosed herein are symmetric, in that the branch arms are of equal length. Dendritic polymers also encompass surface modified dendrimers. For

example, the surface of a PAMAM dendrimer may be modified by the addition of an amino acid, e.g., lysine. It should be understood that reference to any particular type of dendritic polymer as a "polymer," e.g., a "dense star polymer," and "unsymmetrical dendritic polymer," a "cascade polymer" is also intended to encompass bridged dendrimers of that type, dendrimer aggregates of that type, polydisperse dendrimers of that type, and surface modified dendrimers of that type. Polyalkyleneimine (e.g. polyethyleneimine and polypropyleneimine) dendrimers are disclosed as suitable, as are dendrimers of multiple generations (see Figures; column 42-43).

Tomalia does not specifically recite that DAB-AM-16, polypropyleneimine hecadecaamine dendrimer, is surface-modified to include a urea end group.

Aldrich Technical Publication shows that propyleneimine dendrimers are commercially available in multiple generations of diaminobutane dendrimer, including DAB(PA)16.

46,069-9 DAB(PA)4, Polypropyleneimine tetraamine Dendrimer, Generation 1.0  
46,072-9 DAB(PA)8, Polypropyleneimine octaamine Dendrimer, Generation 2.0  
46,907-6 DAB(PA)16, Polypropyleneimine hexadecaamine Dendrimer, Generation 3.0  
46,908-4 DAB(PA)32, Polypropyleneimine dotriacontaamine Dendrimer, Generation 4.0  
46,909-2 DAB(PA)64, Polypropyleneimine tetrahexacontaamine Dendrimer, Generation 5.0

It would have been obvious to one of ordinary skill in the art at the time of the invention to provide urea as an end group on a known PAMAM dendrimer; or a known polypropyleneimine dendrimer, such as DAB-AM-16 disclosed by Aldrich. One would have been motivated to do so because Tomalia teaches that dendrimers can have

terminal groups which are sufficiently reactive to undergo addition or substitution reactions, including e.g. urea. One would have had a reasonable expectation of success in doing so because Tomalia teaches that a variety of dendrimers in varying generation are suitable, including both PAMAM and polyalkyleneimine dendrimers.

Regarding the limitation of claim 1, wherein "the conjugate--upon treatment of protein aggregates with the dendrimer conjugate--causing an increase by a factor of more than 1 in the solubility of protein aggregates over that obtained upon treatment of protein aggregates under the same treatment conditions with a physical mixture of the dendrimer and protein solubilising substance, the physical mixture containing the same molar ratio of the protein solubilising substance to the dendrimer as that in the dendrimer conjugate," it is noted that the instant claims are product claims, not method claims. The recitation of method steps such as "treatment of protein aggregate with the dendrimer conjugate" is not given patentable weight in the instant product claim.

Regarding claims 48-55, Tomalia teaches dendrimers of multiple generations (see Figures; column 42-43) and Aldrich teaches generations 4, 8, 16, 32, 64, etc. which would inherently have the claimed molecular weight. It is noted that the generation number also corresponds to number of surface groups.

Regarding claims 18 and 56-58, drawn to the  $EC_{50}$  value of 10-500  $\mu\text{g/ml}$ , the claims have been examined to the extent that the structure of the dendrimer conjugate  $D(R)_n$  has been addressed. Absent evidence to the contrary, a DAB dendrimer as disclosed by Tomalia having urea as a terminal group would inherently be capable of meeting the claimed functional features, such as  $EC_{50}$  value or protein solubilization,

since a composition and its properties are inseparable. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

*Response to Arguments filed 7/28/2010 regarding Tomalia in view of Aldrich*

Applicant argues on pages 15-17 of the Response that Tomalia et al. describe that the dendrimers can have terminal groups which are sufficiently reactive to undergo addition or substitution reactions (to make conjugates), and examples of such groups for use with STARBURST(tm) PAMAM dendrimers include amino, hydroxyl, mercapto, carboxy, alkenyl, nitrate, allyl, vinyl, amido, halo, urea, etc..., however Applicant argues that Tomalia does not describe or suggest to modify a DAB dendrimer with terminal urea groups for use as a protein solubilizing substance. Applicant asserts that at the time of the invention, neither Tomalia nor Aldrich demonstrated or suggested that there



existed a known problem for which the obvious solution would be to modify a DAB dendrimer with a urea terminal group, and that neither Tomalia or Aldrich provided any other motivation for making the claimed compounds. Applicant further argues that subtle changes to STARBURST(tm) dendrimers result in distinctly different and unpredictable properties, and that one among many groups which are deemed sufficiently reactive to undergo addition or substitution reactions to make conjugates is urea. Applicant asserts that the person of skill in the art wanting to solve the problem of providing protein solubilizing substances would not be motivated by Tomalia or Tomalia in view of Aldrich to arrive at a solution falling within the present claims because neither of these references discusses protein solubilization.

This is not found to be persuasive. In response to applicant's argument that neither Tomalia or Aldrich discuss protein solubilization, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). See also MPEP 2145, II. In the instant case, Tomalia teaches that dendrimer (PAMAM or DAB) can be include reactive terminal groups such as urea. Such compounds can be used to make dendrimer conjugates. Therefore Tomalia provides a suitable motivation for making a dendrimer (PAMAM or DAB) having a urea present on the surface thereof. As set forth in the previous Office Action, the intended use of the compounds for use in protein solubilization is not given patentable weight, since the

intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. It is noted that the instant claims are composition claims, not method of use claims.

### ***Conclusion***

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-

9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

LHS